Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalDec1946uoft

Volume XXIV Toronto, December, 1946 Number 3

The University of Toronto Medical Journal

(AN UNDERGRADUATE PUBLICATION)

This journal is published six times a year, November to April, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to the student recent articles of scientific interest.

$1.50 per volume. 25c. per single copy.

ADVISORY STAFF

PROF. A. E. LINELL, M.D., Ch.B.(Manc)
J. H. COUCH, M.A., M.B., F.R.C.S.(Edin.), F.R.C.S.(C.)
J. HEPBURN, M.B., F.R.C.P.(C.)
D. Y. SOLANDT, M.A., M.D., Ph.D.(Lond.)
A. M. WYNNE, M.A. Qu., Ph.D.
H. H. HYLAND, M.D., M.R.C.P.(Lond.), F.R.C.P.(C)

Editor-in-Chief
R. R. V. RICHTER

Associate Editor
J. E. McBIRNIE

Managing Editor
H. N. CLELAND

Assistant Managing Editor
F. L. CLEMENT

Assistant Editors
E. A. McCULLOCH
M. L. BUNKER

Features Editor
C. L. RODGERS

Abstracts Editor
C. L. ASZKANAZY

Circulation Manager
O. E. LAXDAL

Assistants

1st Year (Premedical)—S. WAX
2nd Year (Premedical)—B. E. PIVNICK
1st Year (Medical)—M. J. T. SEDLMEIR
2nd Year (Medical)—EDWARD FISH
3rd Year—R. W. RUTHERFORD
4th Year—J. M. FINLAY

Address all communications to Room 107, Anatomy Building

CORRESPONDENCE

To the Editor of the University of Toronto Medical Journal.

Sir: The Feature in the October number of this Journal was a clever and sensible bit of advice that I hope may be widely read and deeply pondered. Every student is confronted once with the task of writing thirty-five little essays with a time limit of half an hour each. This comes when he writes for the examinations of the Medical Council of Canada. Next June I will have to read five of these for each of four hundred candidates. I have already read over twenty thousand of these short articles and I am grateful to Mrs. Couch for the help she has given some of the people who will write the next batch.

Her figure of the two triangles is excellent. She did not specify that the angles at the base should be acute and the angle opposite the base should be obtuse. When the article is an answer to an examination question these angles will be so obtuse that the superimposed triangles will closely approximate a rectangle. There is no time for ornamentation or over elaboration at the point of juncture.

The admonition that the article should be brief is well taken provided that brevity be the result of compact statement. The subjunctive mood has little or no place in answering an examination paper. That is one form of essay writing in which the first person indicative is the perfect style. The examiner should be told definitely just what the individual candidate would do under the circumstances suggested by the question.

Every effort is made by the examiners to avoid any ambiguity in the questions set. There are always a few candidates who chide the examiners in a paragraph that used precious time. These are often the people who believe that a wire in the medullary cavity is the only treatment for a fracture of the humerus or that the superior hemorrhoidal vein has nothing to do with hemorrhoids.

The principle of compactness is most often violated by students who make long lists of procedures without indicating the purpose served by the various items, or longer lists of conditions as substitutes for a differential diagnosis. Overdoing the idea of brevity is equally bad. A breathless haste seems to have seized the writer and the reader sees "treat shock: A.T.S.; debridement, skin graft," and wonders who is giving orders or who is doing the work and why and how.

"How to Write an Article" is commended for rereading. Success in writing little essays is a sure promise of success in writing the big ones. There will be thirty-five of the former to write next June.

MALCOLM H. V. CAMERON

The National Society for the Prevention of Blindness announces that papers submitted for the glaucoma prize of $500 offered in 1944 did not conform to the criteria set up by the ophthalmological committee selected to award the prize. Therefore, the prize is again offered for the most valuable original paper adding to existing knowledge about the diagnosis of early glaucoma or the medical treatment of non-congestive glaucoma. The criteria may be secured by writing to the National Society for the Prevention of Blindness, 1790 Broadway, New York 19, N.Y.

Papers may be presented by any practising ophthalmologist of the Western Hemisphere and may be written in English, French, German, Italian, Spanish or Portuguese. Those written in any of the last four languages should be accompanied by a summary in English. Closing date for receipt of papers is December, 1947.

The award will be made by the Society with the guidance of an ophthalmological committee composed of Doctors John N. Evans, chairman; Frank C. Keil, Daniel B. Kirby, John M. McLean, R. Townley Paton, Algernon B. Reese, Bernard Samuels, Kaufman Schlivek, Willis S. Knighton, Manuel Uribe Troncoso, David H. Webster.

AN INTRODUCTION TO GERIATRICS

By E. KREIGER, 4T7

Recently, in the medical profession, geriatrics (that branch of medicine dealing wtih the clinical problems of old age) has aroused interest. The purpose of this article is to introduce this branch of medicine to fellow medical students.

OBJECTIVE:

The primary aim of geriatrics is not to lengthen life, which no doubt it will eventually do; but to enable the aged to live healthier lives—healthier both mentally and physically.

SCOPE:

Geriatrics is concerned with (1) improving the health of the "normal" aged person, and (2) curbing the diseases peculiar to old age.

Before the health of the aged person can be improved, much study must be made on the normal involutionary changes of man. Further knowledge in the science of gerontology (the science dealing with the aging process of life) must be obtained. The pediatrician knows a good deal about developmental changes (part of the aging process and, therefore, a part of the science of gerontology) but comparatively little is known about involutionary changes.

When more is known about normal involutionary changes, the doctor will attempt to improve the "normal health" of the aged individual to the best possible state since "normal health" is just the average health of all our present aged individuals. An analogous situation exists in pediatrics where the doctor seeks to improve the health of the "normal" child by giving him a diet, dosages of drugs and psychotherapy according to the child's state of development.

Diseases peculiar to old age at the present time are difficult to eradicate. Much research is being done on this problem. At the present time, the emphasis is on the prevention and early diagnosis at which stage the present day doctor is in a better position to control or eradicate the disease. The diseases peculiar to old age—the degenerative diseases (i.e. the cardiovascular-renal diseases, arthritis, diabetes mellitus) and cancer, have a far better prognosis when diagnosed and treated early—in people in the forty-to-sixty year age group. When examining patients in this age group, the doctor should inquire about hereditary factors so that he may be in a better position to forestall the manifestations of hereditary diseases in the patient. For example, with a history of cardiovascular disease in the family, the doctor may decide to curb the patient's activities. Industry can play the same role in geriatrics as schools play in pediatrics—i.e. of being the ideal site for routine medical examination of the age group with which that branch of medicine is concerned.

STATUS:

The status of geriatrics at the present time can be compared with that of

"psychosomatic medicine". The term "psychosomatic medicine" emphasizes to the medical profession the integral relation of mind and body. The term "geriatrics" emphasizes the importance of the clinical problems of senescence to the medical profession. Geriatrics is not a specialty, but an integral part of general medical practice. In the future, when much more is known about the clinical problems of senescence, geriatrics will probably take its place alongside of pediatrics as a specialty.

IMPORTANCE:

Since great and rapid strides in the curbing of disease in the young and middle-aged have been made in the last fifty years, more people today are living to ages past fifty and sixty. Since progress in the prevention and the treatment of disease in older people has been almost stationary in the corresponding period, the chances of people, who today reach the ages of fifty and sixty, of enjoying longer and more comfortable lives is only slightly better than it was fifty years ago. Since people past fifty and sixty at the present time suffer from many chronic diseases, the group as a whole in our social structure is a socio-economic liability rather than an asset. To enable the increasing number of people past fifty or sixty to live healthier and more valuable lives, is an important goal of geriatrics.

Since the tendency of our present generation including the medical profession is to regard old age as objectionable and not compatible with physical and mental health, the aged are disgracefully cared for in our society. There should not be private, poorly-run rest homes; there should be publicly-owned, well run homes for the aged. The care of the aged is far below the standard of the care of children. This situation should be corrected.

Actually, the people beyond the age of sixty are, and have been, the leaders of civilization—e.g. in politics, Roosevelt, Stalin, Churchill; in medicine, Osler; in science, Einstein; and in music, Paderewski.

A sound attitude of both the doctor and the layman will not only make old age more comfortable, but will also tend to dispel many of the misconceptions of "objectionable old age".

TREATMENT:

Physical:

The fundamentals of therapy particularly in the physical diseases of old age are (1) correction of etiology, (2) reduction of physiologic burden to the injured tissue, and (3) aid to the tissues' nutrition and respiration; e.g. oxygen and blood. Since at the present time little is known abou the etiology of the diseases peculiar to old age the emphasis in therapy is placed on the latter two fundamentals.

Mental:

In the treatment of mental problems of old age, the medical profession at the

present time can do a great deal more than it is doing to make old age more enjoyable. A summary of important points to be borne in the doctor's mind when confronted with problems of old age as follows:

1. Do not attempt to change, radically, the patient's pattern of life and his habits.
2. Treat the patient as though he were in his prime.
3. Personality traits are emphasized in the aged, i.e. a young fool becomes an old, bigotted scoundrel; a young pleasant, broad-minded individual becomes an old, happy, and respected person.
4. The patient is as old as his outlook—not as old as his chronological age.
5. Keep the old patient active, since mentally and physically the patient deteriorates if he is inactive. Keep him active in spite of minor ills. (The chronological age criterion for retirement in our society is not logical since a person's ability does not always coincide with his chronological age. A fairer method should be devised.)
6. Encourage avocations in early life that will keep the patients active in later life.

If the doctor applies these points in his practice he will have made a substantial contribution toward the improvement of the health of his older patients.

SUMMARY:

In this article, I have attempted to emphasize:

1. The importance of further investigation in geriatrics.
2. That geriatrics is not a specialty, but an integral part of general medical practice.
3. The importance of psychotherapy for the aged.
4. The importance of prevention of disease in the forty-to-sixty age group.

.....

I should like to thank Dr. Trevor Owen for his helpful criticism of this article.

REFERENCES:

STIEGLITZ: *Geriatric Medicine.*
HOWELL: *Old Age*—some practical points in Geriatrics.
WORCESTER: *Care of the Aged, the Dying and the Dead.*

THE PROBLEMS OF THE NATURAL AND ARTIFICIAL MENOPAUSE

By J. C. GOODWIN, M.A., M.D.

Demonstrator in Obstetrics and Gynaecology, University of Toronto

General Considerations: The phase in the life of woman, which for at least one hundred and fifty years has been termed "the change of life", is anticipated by the majority, not only with regret but with fear. The later attitude owes its origin to early medical teaching. An example of this is the following statement made in 1769.* "That period of life at which the menfes ceafe to flow is very critical to the sex. The ftoppage of any cuftomary evacuation, however fmall is fufficient to diforder the whole frame, and often to deftroy life itself. Hence it comes to pafs that fo many women either fall into chronic diforders, or die about this time; fuch of them, however as furvive it, without contracting any chronic difeafe, often become more healthy and hardy than they were before and enjoy ftrength and vigour to a great age". The onus therefore falls upon the modern physician to eradicate such inaccurate concepts. Thus in many otherwise modern women their conscious thinking through such an inheritance becomes overshadowed with ideas of possible mental aberration or nervous derangement which they must take great care to avoid. Other equally ill-defined fears exist such as a change toward masculinity, loss of physical attractiveness, and sundry bodily ailments which they believe will require great fortitude to withstand. They may regard, however, as quite to be expected, irregular or excessive vaginal blood loss; and this in spite of a pervading fear of cancer, with which they associate pain as the indisputable symptom. Their fears are apt either to be aggravated to the stage of extreme nervous excitement over matters of minor consequence, or allayed completely in regard to irregular vaginal bleeding, during an afternoon tea, at which the leading relic of the Victorian era holds forth with the voice of experience. We are apt to be cynical when "old wives' tales" come our way—forgetting the historical fact that the original group of "old wives" were entirely masculine, socially acceptable, and possessors of medical degrees in good standing. Let us then accept our responsibility for the education of modern womanhood as to the truth as we now see it.

Apart from the artificially induced menopause, problems ascribable to the climacteric may arise anywhere from the late thirties to the early fifties. Variability in this age factor exists among individuals and races. We are accustomed to an age range from the forty-fifth to the forty-eighth year in North American women. The duration of so called menopausal symptoms may range from a few months to several years. Women may cease to menstruate abruptly, may skip periods for several months at a time or may show at regular cyclic intervals, a gradual

*Domestic Medicine, or the Family Physician—by Wm. Buchan, M.D.—Edinbury 1769—p. 565

diminution of flow either in amount or duration or both. *Departure from rules must be considered pathological.*

The patient who ceases to menstruate prematurely is very apt to present few symptoms requiring medical assistance—as in this group, genital inactivity tends to be prominent, with associated frigidity, scanty menstruation, sterility, or perhaps a one child family. Few women menstruate after fifty years of age unless reproduction has been almost a continuous process; or sexual activity has been a prominent feature.

Symptoms ascribable to the menopause arise from changes which have taken place secondarily to the physiological cessation of reproductive function, with diminishing pelvic vascularity and increasing atrophy of genital organs. The ovaries become fibrosed. The uterus shrinks in size, becomes sclerosed; the endometrium thins with disappearance of glandular elements—with more gradual atrophic changes occurring in cervical structure and mucosa. The vagina becomes less elastic, fornices flatten, musoca thins and becomes drier. The vaginal orifice shrinks and becomes inelastic. The skin of the vulva becomes paler, less elastic, with loss of labial fat. The rate of development of genital atrophy is entirely unpredictable. Loss of libido is again an inconstant feature—but it is well known that continued sexual activity may delay genital atrophic change quite remarkably, even to ages exceeding sixty.

Associated with cessation of menses symptoms of vasomotor instability appear —with intermittent hot flushes followed by a feeling of coldness. These are aggravated or often induced by the many environmental stresses to which the average woman is subject. Their frequency is related often to the pre-menopausal nervous "make up" of the patient or the abruptness of menstrual cessation. Emotionally stable women however, may show very little evidence that the menopause has taken place and their philosophical attitude becomes a source of encouragement to their more fearful sisters. The role of the gynaecologist in dealing with menopausal problems comes in the investigation and treatment of symptoms due to vasomotor instability, investigation of menstrual abnormalities, and in treatment of conditions related to or associated with varying degrees of genital atrophy.

Treatment of Symptoms of Vasomotor Instability:

Here exclusively symptomatic treatment without a careful evaluation of the patient and her environment is wrong—and yet all too common. The duty of any physician dealing with such problems is clear. Hormonal therapy never should be undertaken without careful pelvic examination, including use of the vaginal speculum. This is true, particularly if any abnormality of menstruation exists. Associated general physical problems may require the help of the internist, just as certain purely gynaecological problems may suggest the assistance of the gynaecologist.

Given an otherwise healthy patient, hormonal therapy for relief of vasomotor symptoms is remarkably successful and requires no complicated method of administration. Treatment should be directed to "tiding the patient over" until

the disturbed metabolism and vasomotor control are restored to the post-menopausal normal. The average patient responds quickly to oral estrogens—though severe symptoms may necessitate intramuscular administration of 5-10,000 I.U. of estrin at four day intervals for rapid control—followed by oral oestrogenic treatment in divided small doses with a gradual reduction in amount given, until control is established without it. Accumulation, toxic, or possible carcinogenic effects may be avoided if the rule of one week without treatment in each month is followed. Furthermore, less oestrin-withdrawal bleeding is associated with this method. If bleeding occurs it is safer to do a diagnostic curettage to rule out early cancer. Until more is known about stilboestrol—a drug possessing "estrogen-like" effects, it is wiser in all probability to use the more natural estrogenic substances which are readily available.

Atrophic Vaginitis

The postmenopausal thinning of vaginal epithelium with a diminished blood supply renders the vagina more liable to surface infection. Areas of denudation may develop following coitus, due to lessened cervical secretion and a drier vagina. Symptoms of vaginal discharge, burning, vulvar irritation, dyspareunia, dysuria appear, and occasionally spotting of blood. The vaginal discharge is thin and mucopurulent—vulva and vaginal walls are red and tender on examination. The occurrence of spotting naturally requires careful investigation—and if areas are not readily evident within the vagina, which bleed easily on examination, diagnostic curettage should be advised; even though no other pelvic abnormality is apparent, in view of the possibility of early carcinoma of the body of the uterus. However, if the local picture justifies it a period of treatment and further observation may be undertaken.

The local condition as a rule is improved quickly with one or two applications of 5-10 percent Silver Nitrate to the entire vaginal surface—followed by the daily use of vinegar douches: 5 tbs. to 1 quart of warm water. This may be followed in 2 weeks by the nightly use of vaginal suppositories containing 1000-2500 I.U. of estrin for 1-2 weeks, in more severe cases. Narrowing of the vaginal orifice due to atrophic change may necessitate plastic enlargement if the patient's husband is sexually active; or in the case of a widow who remarries a younger man. Here local and oral estrogenic therapy may have to be continued as well.

Atrophic Endometritis:

As a symptom-producing entity, this is probably quite rare—though it may be associate of atrophic vaginitis. Symptoms of thin vaginal discharge and spotting may be due to this cause. Cases of vascular hypertension may bleed from an atrophic endometrium. Curettage obviously is required to establish a diagnosis: and in such cases scanty or even no endometrium may be obtained.

Genital Prolapse:

This becomes evident more often after the menopause, due to diminishing pelvic

blood supply and loss of tissue tone. If the general physical condition is satisfactory, gynaecological surgery is indicated, rather than subjecting the patient often to years of pessary treatment. The necessity of douching and changing pessaries at regular intervals is apt to prove a source of annoyance to many women. Atrophic vaginitis may be induced or aggravated by pessary treatment, unless regular care is given.

Kraurosis Vulvae:

Superadded upon the normal postmenopausal atrophy of the vulva, there may occur a more extensive and more rapidly developing atrophic state—affecting only the labia minora, vestibule and vaginal orifice. This is known as Kraurosis vulvae. It is not related to leucoplakia—though sometimes confused with it; and furthermore bears no relation to cancer. In its early stages the surface becomes shiny red with patches of deeper redness. The surface is painful, with discomfort on walking; and marked dyspareunia develops. Itchiness is not a symptom. Later the surface becomes yellowish-white, and subcutaneous connective tissue contraction appears to a remarkable degree. This later becomes quiescent with extensive fibrosis of deeper tissues, and sometimes with extreme stenosis of vaginal orifice. Oestrogenic therapy may be of benefit if given in massive doses—though it may only delay the ultimate atrophic process. The local discomfort, however, may be alleviated by local applications. Plastic enlargement of vaginal orifice is usually required if sexual relations are to continue.

Leucoderma Vulvae:

This harmless condition is due to atrophy of the cutaneous pigment cells. Symmetrical areas of skin on each side of vulva may be involved. The surface otherwise is unaltered and there are no symptoms. It is mentioned only because it may be confused with leucoplakia of the vulva.

Leucoplakia Vulvae:

This important gynaecological condition is usually reported by the patient because of severe pruritis of the vulva, which develops early; and later becomes intense in over 90 percent of cases, with burning genital discomfort, and dyspareunia in the symptomatic background. It is a chronic atrophic inflammatory process, resulting in a thickening of the epithelial surface of the area of the vulva involved. In its early stage it may resemble Kraurosis. The cases which improve under oestrogenic therapy in my opinion are more likely to be Kraurosis vulvae and not leucoplakia. Leucoplakia may affect the vulva either partially or entirely. It is characterized by the formation of plaques of thickened keratinized epidermis—which present at bluish-white or grey appearance. Eventually fibrosis of the subepithelial tissue reduces the blood supply. Flattening of surface anatomy results and the labia minora may become ridge-like. A cracked "parchment-like appearance" develops with small points of ulceration which proceed quite commonly to

cancer. Malignant change may be delayed, but well marked leucoplakia presents too great a risk to justify prolonged observation. The intense pruritis usually fails to respond to local treatment. Oestrogenic therapy except in the early stage is not justifiable—and should not be employed unless the vulva is inspected at frequent intervals during treatment. Vulvectomy is the treatment of choice in the well established case.

Artificial or Pathological Menopause:

By this is meant menopausal symptoms which are induced following surgical removal of uterus and ovaries; or following radium or x-radiation in amounts sufficient to produce cessation of menstruation. Vasomotor symptoms in patients who are within a few years of the natural menopausal age, may be more severe than following the normal climacteric—probably due to the abrupt termination of menstrual function. They usually respond well to estrogenic treatment given according to the plan outlined above. If, however, the patient has been under treatment for pelvic cancer or pelvic endometriosis, control of vasomotor symtoms should be undertaken *without* the use of estrogens or stiboestrol in any form.

In younger women vasomotor symptoms following artificial induction of the menopause are apt to be mild; and vulvo-vaginal atrophic changes are definitely slower in development, and may not be apparent for many years. This is particularly true if coitus is continued regularly. Vasomotor control may be easily established; with instability again apparent around 45-50 years of age. This would suggest that regression of thyroid, pituitary or adrenal function is not dependent solely upon absence of ovarian tissue or ovarian activity; but rather to additional factors dependent upon age—i.e. to the metabolic, vascular or endocrine changes which occur at the *normal* time of the menopause.

CHOLECYSTITIS

GERALD S. MARGULIES, 4T7

Incidence (1)

Obesity and multiple pregnancy are predisposing factors. The ratio of females to males is 2:1. The adage "fat, female, fertile and forty" has much truth behind it, however many cases do not fit into this classical picture.

Slightly more than one-half of adults past thirty years of age have abnormal gall bladders and approximately one-fifth have gallstones. However, the reported incidence of clinical cholecystitis is less than this, and depends on statistics from various clinics based on surgical material.

Acute Cholecystitis

There are three chief factors concerned in the production of Acute Cholecystitis.

1) Obstruction. This is the most important etiological factor. Graham (2) of Toronto states that no case of acute cholecystitis in his experience has ever occurred in which there was not obstruction of the cystic duct either from stone or thick tarry bile. Wolfson and Rothenburg (3) noted in reviewing the literature that 4 to 30% of cases of surgically verified acute cholecystitis are not associated with the presence of stones. However, in the majority of cases there was a definite history of either an acute respiratory infection or some other infectious disease immediately preceding the onset of symptoms. It is reasonable to suppose that in many of these latter cases mild inflammation of the bile ducts, particularly the cystic duct, would cause the obstruction and initiate the cycle of ensuing events; in the others primary haematogenous infection would be the cause. A fair estimate by most authors is that 90%-95% of cases are associated with obstruction.

2) Invasion by organisms of high virulence.

3) Interference with the vascular supply.

Pathological Considerations

McKenty (4) gives the best classification for practical purposes. He divides acute cholecystitis into (1) an uncomplicated stage, and (2) stage of complications.

1) Uncomplicated Stage. The stone becomes impacted in Hartman's Pouch or the cystic duct and obstructs the outflow of bile, a chemical irritant. The gall bladder becomes distended and its walls thickened, edematous, and infiltrated with round cells chiefly, and a few polymorphs. The serous surface is congested, covered by a fibrinous exudate and the mucosa is bright red or purple and sometimes ulcerated. The distension of the gall bladder and edema of its wall are due both to exudation and transudation. The exudation is an inflammatory reaction due to the imprisoned bile which, for some unexplained reason, is a chemical irritant only when its outflow is obstructed. Increased concentration of bile alone with free outflow will not cause the same reaction. The transudation is caused by the

impacted stone obstructing lymphatics and veins draining the gall bladder wall, and by contraction of unstriated muscle fibres compressing mucosal veins and capillaries as the obstructed gall bladder goes into spasm.

In the majority of cases, with conservative treatment, resolution occurs with some resulting fibrous thickening of the wall, the impacted stone either having been passed or falling back into the gall bladder. Should the stone remain impacted for many days and bacterial invasion not occur, then the rare condition of mucocele of the gall bladder results, the bile being completely absorbed and the gall bladder distended with exudate and transudate. Should bacterial invasion occur, then the stage of complications is entered.

2) Stage of Complications. In about five or six days on an average, the acutely inflamed, edematous wall becomes invaded by pathogenic micro-organisms, chiefly B. coli and streptococci. The origin of these micro-organisms has usually been assumed to be haematogenous. The idea is gaining ground however, that these organisms come from the bile itself. In other words, a few organisms in the bile of a normal gall bladder are harmless, whereas they may invade an edematous, obstructed gall bladder. Another possibility, though less likely than the above two, is invasion of organisms from a neighboring viscus, particularly transverse colon. A definite time limit, however, cannot be too rigidly set, as occasionally a gall bladder may become gangrenous within twenty-four hours of the onset of symptoms.

During this stage, the following sequence of events may occur: The gall bladder contents become frankly purulent, a condition of empyema of the gall bladder. This may resolve with conservative treatment or go on to gangrene of the gall bladder wall, either local or general. Perforation will then result usually with a localized pericystic or subphrenic abscess, since the process is slow and walling off by the greater omentum and adjacent structures usually has time to occur. A localized abscess containing stones may be so completely walled off, that it will give no further trouble, merely a pocket of stones resulting. Generalized peritonitis from ruptured gall bladder though sometimes occurring is uncommon.

Clinical Picture

1) Pain. The initial pain is that of so called biliary colic due to obstruction of the cystic duct and distension of its wall. Careful questioning of the patient will reveal that it is a steady pain, not truly colicy in nature as the gall bladder, unlike the intestine, has not sufficient musculature to attempt to overcome the obstruction by rhythmical contraction. It is situated in the epigastrium or right upper quadrant. This often radiates through to the back just below the inferior angle of the scapula, and in about 5% of cases to the same shoulder. Later the pain in the right upper quadrant is due to inflammatory involvement of the peritoneum.

Thus to clarify—pain lasting only a few hours is referred to as gall bladder colic but if it lasts approximately over twelve hours it is called acute cholecystitis, the gall bladder wall having become inflamed.

2) Vomiting—in 85% of cases.

3) Localized tenderness in the right upper quadrant.

4) Murphy's sign. The examiner palpates the right upper quadrant while the patient takes a deep inspiration. Sudden arrest of inspiration due to the impingement of the inflamed gall bladder against the examiner's hand constitutes a positive sign. This is an extremely useful and practical test.

5) The gall bladder is distended and palpable in 20% of cases.

6) Rigidity. This is usually a voluntary rigidity by the patient rather than a true rigidity.

7) Jaundice in 10% to 15% of cases. This is due to one of the following possibilities:

(a) Stone in the common bile duct.
(b) Pressure of Hartman's Pouch on common bile duct.
(c) Edema from the gall bladder extending to the common bile duct.
(d) Pressure of enlarged cystic gland on the common bile duct is a possibility, though uncommon.

8) Previous history of fat intolerance.

9) Leucocytosis—12,000-20,000.

10) Temperature from 99-101° F.

Should empyema or gangrene develop, these signs and symptoms are accentuated with increased pain, local tenderness, fever, a rising pulse rate, and probably a definite palpable mass. The onset of jaundice with true rigors and high temperature is very serious and usually indicates an accompanying cholangitis.

TREATMENT

This is somewhat controversial, particularly as regards to the time of surgical intervention.

Acute cholecystitis is not a surgical emergency. This is in contrast to acute appendicitis. In the latter we are dealing with a septic tank full of pathogenic organisms whereas in the former the gall bladder may be relatively aseptic for the first four or five days. At Toronto General Hospital (5), in a series of 164 cases treated by delayed operation, the mortality was 4.2%. Hence when the patient is first seen in the presence of an attack of acute cholecystitis, one can devote several hours to restoring the biochemical balance by administration of intravenous glucose in saline. Morphine, rest and heat to the abdomen are ordered to overcome pain and fatigue and the patient is fully investigated for associated conditions such as heart disease, diabetes, etc. If following this procedure the pain persists and increases, with increasing local tenderness, or the pulse rate increases or remains high, which suggests empyema, or jaundice and chills occur suggesting cholangitis, then conservative treatment must be abandoned and surgical intervention undertaken as soon as the patient's biochemical balance is corrected. Usually however, under this conservative regime there is marked clinical improvement.

Should the patient definitely improve, the question then arises when and if surgery should be undertaken. If this is the patient's first acute attack, then cholecystectomy is not justified, as there are many cases on record in which the

patient had one acute attack and was symptom free for the rest of his life.

If the patient has a history of previous acute attacks suggestive of stones obstructing the cystic duct, then if the patient is seen within the first 72 hours following the onset of the attack, operation is advisable at this time rather than delay several weeks till the acute inflammation has subsided, chiefly for the following reasons:

1) The operation is fairly easy at this time as the gall bladder can be shelled out of its bed along a line of cleavage. Later, adhesions may complicate matters.

2) The gall bladder wall though inflamed has not yet been invaded with pathogenic organisms during this initial period, and there is little danger of infection.

3) Perforation causing general peritonitis, though uncommon, may occur.

3) Economic Factor. Patient can be operated upon just as safely with only the one period of hospitalization. Also, if sent home, he frequently stays home from work during the intervening six weeks.

5) Early intervention tends to avert damage to the rest of the biliary system, e.g., cholangitis, pancreatitis.

Though early operation is desirable, in over half the cases, the patient is not seen within the first 72 hours. If not operated upon, the patient is discharged from the hospital when he is in a satisfactory condition, put on a bland low fat diet, and then returns in about six weeks for cholecystectomy.

Although some surgeons quote figures pointing to the advantage of early operation when the patient is seen early, while others are equally convincing in their advocacy of delaying operation whenever possible, so far as mortality rates are concerned, in expert hands, the resuts of early or late operation are about the same.

Cholecystostomy should only be done in those cases in which cholecystectomy would be an unwarranted risk, e.g., due to old age, or associatel illness of patient, severe empyema of the gall bladder, or cholangitis. In these few cases the gall bladder is drained and the stones removed.

At operation, the question will arise as to whether or not the common bile duct should be explored. The gall bladder should not be removed until after the necessary treatment of the common and hepatic duct has been carried out, because the cause of obstruction may be carcinoma of the head of the pancreas, or ampulla of Vater. In this case a cholecystgastrostomy is a much easier procedure than anastomosis of the bile duct to the stomach or bowel. Walters of Mayo Clinic found stones in the common bile duct in 15% of cases—which had stones in the gall bladder, while Lahey of Boston claims an 18% incidence. Stones may be present in the common bile duct without colic or jaundice, the so called silent stone. Opening and exploration should only be done in cases with one or more of these well established indications. (6.)

1) History of jaundice—particularly repeated attacks.
2) Fine sand or multiple small stones palpable in the gall bladder.
3) Dilated common bile duct.
4) Palpable stone in common bile duct.

5) Thickening of the head of the pancreas, since the impacted stone in the ampulla of Vater will cause chronic pancreatitis. Before opening the common bile duct a needle should be inserted and a small quantity of bile aspirated to make sure that it is not the portal vein, when structures are distorted. After exploration a T tube is left in to decompress the duct and prevent leakage.

Chronic Cholecystitis.

This can be classified into two types:

1) A rather vague syndrome in which there is fat intolerance, epigastric fullness after meals, bloating and gaseous eructations, and nausea. These are gastric symptoms, due to pylorospasm and abnormal gastric motility, the stomach and gall bladder having the same double nerve supply (Vagus and Sympathetic Th9). A few words about treatment are important in order to emphasize that surgery in this type of case is entirely unsatisfactory. Follow up investigation at Barnes Hospital (7) showed that 35% of patients with a diseased but non calculous gall bladder and presenting merely symptoms of dyspepsia remained unrelieved following removal of the gall bladder. Medical treatment with a low fat, bland, weight reducing diet, control of constipation, judicious use of antispasmodics and sedatives, and non surgical biliary drainage with concentrated magnesium sulphate solution, is usually helpful.

2) In addition to the above picture, there may be a history of repeated acute incidents, i.e., acute cholecystitis is usually superimposed on a chronic cholecystitis, each acute incident causing increased edema and then fibrosis. It is in these cases with stones that surgery is so satisfactory, as has already been described.

Illustrative Case.

This 46-year-old woman had epigastric pain for 16 years, ½ hour after meals and lasting 2 to 3 hours, aggravated by milk, cold water and fried and fatty foods. It was associated with a feeling of fullness and belching of gas.

For the past 2 months, the pain was more severe and sharp, radiating through to the back, accompanied often by nausea and vomiting and followed by a dull aching sensation in the epigastrium which lasts 2 or 3 days. These attacks occur about once every two weeks. Accompanying these attacks, the skin is slightly yellowish in colour 1 day or so before the pain starts, and lasts 3 or 4 days following and is associated with itchiness. The urine is dark during the attacks, stools are normal in colour and frequent fullness and belching occur after her meals.

Examination: Abdomen is obese and flaccid, no masses but generalized tenderness, more marked in the right upper quadrant.

X-ray—no filling or concentration of dye in Graham's visualization test. Hence there is no visualization and no *radio-opaques* stones.

At operation the gall bladder was enlarged and full of facetted yellowish brown stones, the common bile duct was largely dilated. The duct was explored and two

large hard stones removed. A T tube was inserted and the abdomen closed.

Pathological Examination. Slightly thickened gall bladder wall, greyish pink mucosa, yellowish grey serosa. Wall is edematous infiltrated with lymphocytes, plasma cells and eosinophils and some diffuse fibro-fatty overproduction in the submucous layer. B. coli cultured from the bile and seen as gram negative bacilli in direct smear.

It will be readily appreciated by the reader that cholecystitis is a rather controversial subject. However, clarity has been sought by avoiding controversy as much as possible. Every case must in the final analysis be considered a law unto itself after following certain principles.

I should like to sincerely thank Dr. F. G. Kergin for his constructive criticism and helpful suggestions during the preparation of this article.

BIBLIOGRAPHY

(1) Lichtman—Diseases of Liver—Gall Bladder and Bile Ducts—p. 818.
(2) Graham, R. R.—Acute Cholecystitis—Am. J. of Surg., N.S. 46, Dec. 1939.—p. 589.
(3) Wolfson, W. L. and Rothenburg, R. E.—Acute non calculous Cholecystitis, J.A.M.A. 106: June 6, 1936.
(4) McKenty—Acute Cholecystitis—C.M.A.J.—1938—Vol. 38, p. 236.
(5) Graham, R. C.—Surgical Procedures on Biliary Tract—Nova Scotia Medical Bulletin, Oct. 1943.—p. 227.
(6) Peikoff, S. S.—Post Cholecystectomy Syndrome—Manitoba Medical Journal—vol. 26.
(7) Graham, E. A. and McKay, W. A.—Consideration of the Troubles of the Gall Bladder, J.A.M.A. 103: 1497, 1934.

SIGNIFICANCE OF THE LIVER IN PROTEIN METABOLISM

E. A. SELLERS, M.D.
Assistant Professor of Pharmacology

General

In a review of the significance of the liver in protein metabolism, some discussion of proteins, and protein metabolism generally, seems necessary. Proteins are among the most complex of the biological constituents of cells. Besides carbon, oxygen, hydrogen and nitrogen, they may contain sulphur and sometimes phosphorus. Substances which can be classed as proteins have been obtained with molecular weights varying from 1,000 to 300,000,000. The molecule is made up of many units of amino acids joined together in primary valences through their amino and carboxyl groups—the peptide linkage. Twenty-two or twenty-three amino acids of nutritional significance have been found in animal and plant proteins. Some proteins contain all, while others may be lacking in one or more of them. The actively metabolizing proteins of living tissues are probably bound to each other by their polar side chains and to non-protein cellular constituents by secondary valences. It is probable that these labile proteins have a loosely knit fibrous structure which readily breaks down on chemical manipulation to yield the isolated proteins, the composition and properties of which depend in a measure on the reagents employed in their preparation.

Essential Amino Acids

Certain of the amino acids are necessary for normal growth, the maintenance of nitrogen balance and reproduction or other special functions. They also may be essential components of chemical reactions—for instance, the oxidative enzyme reactions, or the transmethylation reaction in which the labile methyl groups of methionine unite with ethanolamine to form choline.

Rose, and Rose and Cox have defined an essential amino acid as one which cannot by synthesized by the animal organism of material ordinarily available at a speed commensurate with demands for normal growth. The "essentiality" is linked with the general metabolic rate. As might be expected, therefore, the dividing line between essential and non-essential acids is not entirely clear cut. If specific functions, rather than growth, are selected as criteria of essentiality, or if tests are conducted with different species, some variation in the list of essential and semi-essential acids is obtained. The non-essential acids, and some of the essential acids, can be synthesized in the body from other nutrients. In large part at any rate, this occurs in the liver.

Utilization

After digestion in the stomach and small intestine, during which protein is

Presented before the Physiological Society, University of Toronto, January, 1945.

broken down by hydrolytic enzymes into amino acids, absorption takes place. Most amino acids are carried directly in the blood stream, although the level in the thoracic duct also rises. If protein or amino acid complexes are absorbed as such, they must be changed into amino acids in passing through the intestinal wall, as such substances are not found normally in blood. Under some circumstances, certain proteins, e.g., egg white, can be absorbed direct, but this is not usual. The amino acids of the blood may be used for synthesis of body protein, or they may be deaminated in the liver, kidney, or intestinal mucosa. *Deamination* is believed to occur by a process of α-oxidation, i.e., oxidation of the carbon atom to which the amino group is attached, with the production of an α-ketonic acid. Subsequently, oxidation in the α position again may occur producing CO_2 and a fatty acid with one less carbon atom.

$$\text{e.g. } \underset{\alpha \text{ amino}}{R.CH_2.CHNH_2COOH} \xrightarrow{\text{oxid.}} \underset{\alpha \text{ ketonic}}{R.CH_2CO.COOH} + NH_3$$

$$\underset{\alpha \text{ ketonic}}{R.CH_2.CO.COOH} \xrightarrow{\text{oxid.}} \underset{\text{fatty acid}}{R.CH_2.COOH} + CO_2$$

The amino group is split from the amino acid molecule and the ammonia so produced is combined with CO_2 to form urea, which is excreted in the urine.

Mann and McGath and their associates have shown that the liver is the principal site of urea formation. After hepatectomy injected amino acids do not raise the blood urea in dogs—in fact the level steadily falls after complete removal of the liver. In the intact animal, in perfusion experiments, or using liver slices when amino acids are introduced, urea is produced. Arginine is capable of being hydrolyzed directly to urea and ornithine. Some doubt still exists as to the cycle by which this takes place.

Glycine, alanine, aspartic, glutamic and hydroxyglutamic acids, serine, cystine, arginine and proline are capable of undergoing the transformation to glucose. With the exception of arginine and proline, these are all straight chain amino acids with less than 6 carbon atoms. According to Bollman, Mann and McGath, the conversion process occurs only in the liver. The evidence in support of this is based on the observation that glycine or others of these acids injected in the hepatectomized animal does not affect the hypoglycemia which exists in such cases.

Theories of Protein Metabolism

According to the classical theory of protein metabolism, presented by Folin, protein synthesis in the adult organism in nitrogenous equilibrium was restricted to the replacement of an unceasing "wear and tear", or endogenous quota. This endogenous quota corresponded approximately to the minimum excretion of nitrogen on a diet containing little or no nitrogen but which was otherwise adequate. When more than this minimal quantity of nitrogen was ingested, the excess over the

endogenous requirement was quickly catabolized and appeared in the urine mainly as urea. The experimental basis for the theory of a "wear and tear" quota was Folin's discovery of the constancy of the urinary creatinine and neutral sulphur excretion regardless of the amount of protein in the diet. The excretion of neutral sulphur and creatinine was believed to represent the "wear and tear" of tissue protein. These were therefore considered as a measure of the rate of endogenous nitrogen metabolism, and th excretion of urea to represent the catabolic products of dietary protein only.

McCollum and Osborne and Mendel doubted that the "wear and tear" quota really involved destruction of intracellular protein. They suggested that endogenous metabolism supplied essential amino acids, when these were not present in the diet.

In 1935 Borsook and Keighley proposed a theory of protein metabolism which was completely opposed to previous modifications of Folin's theory. In an animal in nitrogen equilibrium, breakdown of intracellular protein progresses continually, even when adequate quantities of amino acids are available from the diet. The amount involved is greater than Folin's endogenous quota, and is proportionate to the level at which the nitrogen balance has been set by the previous dietary history. In nitrogen balance therefore, a corresponding quantity of amino acids is *synthesized* into tissue protein. After the ingestion and hydrolysis of protein, some of its amino acids contribute to maintaining a concentration of free amino acids in the blood and tissues. A large fraction is synthesized into protein and peptides, while the remainder is catabolized.

Storage

A fundamental discrepancy to the classical theory is in the phenomenon of "labile nitrogen" or "reserve" protein, for it has long been known that when a starved animal is fed it retains a large part of the ingested protein. It was presumed that such protein was held in some hypothetical depôt. Although protein can be stored, the term labile or reserve protein implies a difference from other protein. There is no evidence that "reserve" protein differs from the main mass of body protein. It may be that "labile nitrogen" is not distinguished by a difference in composition but by a difference in location. Some organs, the liver, intestine and kidney, change in protein content rapidly with changes in level of dietary protein, but these organs can increase or decrease only within certain limits. With a continued fast or low nitrogen intake, as the lower limits of size of the more labile organs are approached, larger amounts of nitrogen will come from the organs slower to change, such as the muscles. Thus in the course of a fast, the source of reserve protein will shift from organs which change rapidly to those which change slowly and hence its composition and the nitrogen-sulphur ratio in the urine will change.

Liver Proteins

Madden and Whipple showed that a dynamic equilibrium exists in the body

whereby proteins of the plasma, liver and other tissues are constantly changing. Schoenheimer and his group, by using N^{15} as a tracer, produced direct evidence that nearly all the proteins of the body are continually undergoing synthesis and breakdown. In the liver and intestinal mucosa more than half the tissue protein is broken down and re-synthesized within 10 days. In the muscles the change is slower, and it is still slower in the erythrocytes. Schoenheimer showed that labelled glycine, l-leucine, d-leucine and dl-tyrosine in the diet were incorporated with approximately equal rapidity in the proteins of plasma, kidney, liver and intestinal tract. This is true of all the proteins of plasma and of anti-body protein produced by active immunity reactions. Anti-body protein injected (passive immunity) does not incorporate amino acids from the diet.

Addis, Poo and Lew showed that after a fast of two days, rats lost 20% of the protein content of their livers, while protein loss in other organs amounted to only 4%. Kosterlitz and Cramb by correlating the loss of phospholipid and nucleoprotein with liver protein loss showed that there is no loss in *number* of cells, but decrease in *volume* of each cell. The liver protein must have been metabolized, or at least transported, to fulfill other more urgent needs of the body. After such a fast, as has been pointed out, there is little loss from other protein stores. "Liver proteins are in a state of constant flux as incoming materials are synthesized into protein and outgoing protein (e.g. fibrinogen and prothrombin) is constantly supplied to fill urgent body requirements. There must be some modification of liver protein to produce plasma proteins, just as plasma proteins must be modified slightly when they supply the needs of body cells. This implies that liver proteins have a variable make up—that these proteins are part of a dynamic system—that certain amino acids may be lost or regained without serious disturbance of cell function."

Blood Proteins

Observations on the function of the diseased liver have afforded information on the relationship of the liver to the blood proteins. In cases of extensive liver disease, marked changes in the plasma proteins are noticed. A decrease in the production of albumen with sometimes a reversal of the AG ratio occurs three to four hours after hepatectomy.

A drop in all plasma proteins takes place, the percentage decrease being about equal for albumen and fibrinogen (35%) and less for globulin (17%) (Canto). A fall in fibrinogen level in toxic hepatitis, or after hepatectomy was shown to occur by Drury and McMaster (1929), Mann and Bollman (1929) and Jones and Smith (1930).

Whipple and Robscheit-Robbins have shown that human liver with diseased parenchyma is less effective in promoting haemoglobin formation than normal liver. They believe that this indicates a decreased storage of the anti-secondary anemia factor. The presence of an anti-secondary anemia factor controlling haemoglobin formation, as well as an anti-pernicious anemia factor controlling erythrocyte stroma

formation is fairly generally accepted. Their *nature* is not known, yet their control of this phase of special protein synthesis is clear. In advanced chronic liver disease anemia, sometimes macrocytic, often occurs.

Effect of Low Protein on Liver

So far, the influence of the *liver* on protein metabolism has been discussed. Some consideration of the effects of *protein lack* on the liver is appropriate.

When the amount of protein ingested is decreased below a critical level, infiltration of fat or liver damage occurs. The level depends on the type of protein and to some extent on other factors present in the diet. For instance, fat, especially cholesterol, or cystine, increase the deposition of fat in the liver.

In 1935, while investigating the curative action of choline on the fatty livers of rats, Best and Huntsman had occasion to feed their animals with a diet consisting entirely of sucrose. They observed that the liver became even more fatty. When the experiment was repeated, replacing 20% of the sugar with an equivalent amount of casein, the increase in fat was not found.

In 1937, Tucker and Eckstein discovered that methionine was lipotropic and was probably responsible for a large part, if not all, of the activity of casein in this respect. Best and his collaborators, Channon, and others, had previously shown the lipotropic activity of choline and betaine, and the antilipotropic effect of cystine. Beeston and Channon, Singal and Eckstein showed that other amino acids did not possess the lipotropic activity of methionine. Thus it appeared that the deposition of fat in the liver depended not on the level of protein intake but on the level of lipotropic factors in the diet.

Cirrhosis

Long term experiments have brought to light some new, and, in some respects, more significant details of the effect of deficiencies of lipotropes and related food factors in the pathogenesis of liver disease. In 1938, Chaikoff, Connor and Biskind reported that eight of sixteen depancreatized dogs treated with insulin, and fed a diet of lean meat, sucrose, bone ash and certain vitamin supplements developed hepatic fibrosis. The earliest evidence of hepatic fibrosis was observed one and a half years after pancreatectomy. Connor and Chaikoff reported the same year that cirrhosis of the liver in intact dogs occurred when the feeding of large amounts of alcohol was superimposed upon a previously established fatty liver. It was subsequently shown by the same authors that, even in the absence of alcohol, "the continued presence of excessively high amounts of fat in the liver for several months stimulates hepatic fibrosis even in normal dogs to the extent that it may be called true cirrhosis and cause the death of the animal".

During the same period, similar work was going on in other laboratories, using other experimental animals and techniques. Hepatic cirrhosis in rats resulted from feeding a low protein diet. By giving 20% alcohol to drink in place of water, the fibrotic process was accelerated. By means of a deficient diet, Rich and Hamilton

produced cirrhosis in rabbits and reported its prevention by yeast. In the course of investigations into the effects of vitamin B deficiencies, Gyorgy and Goldblatt observed "fatty degeneration, focal and massive necrosis, hyperemia, haemorrhage and in some cases perilobular and condensation fibrosis" in the livers of rats on a diet deficient in several essential food factors. That at least *some* of these lesions were attributable to a choline deficiency was indicated by Blumberg and McCollum in 1941 when they found that choline prevented hepatic cirrhosis in rats fed a high-fat, low-protein diet. Methionine retarded the cirrhotic process. The preventive action of choline in experimental dietary cirrhosis has since been repeatedly confirmed.

The time required for dietary cirrhosis to develop varies with the circumstances. In one group of experiments the time necessary to produce cirrhosis in rats averaged less than three months, some animals becoming cirrhotic in as short a time as five weeks. This is in distinction to the appearance of fatty livers which has been observed in rats within a few days of starting the offending diet.

Descriptions of the cirrhotic and necrotic types of dietary liver injury have been given by Lillie and co-workers; Gyorgy; Himsworth and Glynn and others. The nature of the lesions depend on the precise composition of the diet. In the gross, the surface of the liver may be discolored and mottled with a rough nodular appearance, but, not infrequently, the surface of the liver is relatively smooth and gives no indication of the degree of fibrosis.

Microscopically, the earliest evident change, as would be expected, is the appearance of fat globules of varying size in the liver cells. A fibrosis commences later, and is mostly periportal. Later still, the fibrous trabeculae segregate nodules of fat-laden cells. The segregated areas not infrequently contain apparently normal portal areas with duct, vein, and perhaps artery even in advanced cirrhosis. In places, the trabeculae broaden out into bulky areas of replacement of hepatic parenchyma. When extensive necrosis of liver cells occurs it is usually central and mid-zonal in location.

A most frequent finding in cases of experimental cirrhosis of dietary origin is the presence of globules of a peculiar hyaline, basophilic substance which takes up fat stains. The chemical composition of this material, called "ceroid," has not been discovered. Ceroid may also be found in the lung, spleen and other organs. For some time considerable significance was attached to its presence in experimental cirrhosis because it does not occur in human cases of the disease. Recently, this discrepancy has been removed by the observation that if the cod liver oil, which is usually given in diets to supply vitamins A and D, is replaced by the purified vitamins, no ceroid is formed.

Replacement of lipotropes in the diets of cirrhotic rats is followed by the disappearance of fat in the liver cells and a marked increase in their size, and apparently in their number, with the formation of hyperplastic nodules. Complete disappearance of the fat may occur in 16 to 18 days. Regression of the fibrous changes, however, is not so evident.

Daft, Sebrell and Lillie were the first to report experiments which were inter-

preted to indicate the respective roles of methionine, choline and cystine in preventing dietary hepatic injury. They state "choline (and methionine, a choline precursor) has a preventive action in the development of hepatic cirrhosis and the sulphur-containing amino acids, methionine and cystine, have a preventive action in the development of hepatic haemorrhage and necrosis. This suggests that the cirrhosis and the haemorrhage and necrosis are separate and distinct entities." The position of cystine, which is not a true lipotrope, in the choline, methionine, cystine triad is peculiar inasmuch as, when fed in excess, it may itself cause hepatic cirrhosis. Recently, Himsworth and Glynn have corroborated the conclusion of Daft et al and extended its experimental basis. According to these authors "dietetic hepatic necrosis is a deficiency disease caused by deficiency of a component of protein and prevented by administration of methionine . . . . neither the carbohydrate, fat, vitamin, mineral nor choline content of the diet exert more than, at most, a modifying influence." When the diet of experimental animals contains insufficient sulphur-containing amino acids, the massive hepatic necrosis which ensues has many points in common, clinically as well as pathologically, with acute yellow atrophy of the liver in man. The experimental disease may be fatal or the animal may recover spontaneously without any change in the dietary regimen. In the latter case, the liver becomes heavily scarred and grossly irregular. This belief, that massive hepatic necrosis is due to a deficiency of the sulphur-containing amino acids, is backed by strong experimental evidence. Hock and Fink, working independently in Germany, came to this same conclusion in 1943. From the evidence at hand it is postulated that portal cirrhosis of dietary origin is due to a deficiency of choline or precursors of choline. However, in spite of the work cited above, the evidence (1947) that massive liver necrosis is due *solely* to a deficiency of the sulphur-containing amino acids, is not so convincing. Attempts to repeat the work of Himsworth and Glynn have not been successful. In addition, the belief that "necrosis" and "cirrhosis" are distinct entities has not gained universal acceptance. It seems more likely that a difference of degree rather than pathogenesis may account for the differing pathological appearance.

Not only may lipotrope-deficient diets give rise to hepatic injury independently, but there is clear experimental evidence that the lipotropes influence the susceptibility of the liver to various hepatic toxins. Barrett and co-workers found that rats maintained on a choline deficient diet developed very fatty livers during the 20-day period following the administration of carbon tetrachloride. Almost normal livers resulted at the end of that time in another group of poisoned animals fed with the same basal diet but with added choline. Miller and Whipple depleted dogs of protein (and, therefore, of cystine and methionine) but not of choline and found that these animals had many times the sensitivity of normal dogs to chloroform poisoning. The increase in sensitivity could be abolished by feeding a high protein meal, methionine or choline plus cystine before the exposure to chloroform. Methionine and choline plus cystine were also active therapeutically. Similar observations were made by Hawkins and co-workers in the case of mapharsen and arsphenamine poisoning. Recently Sellards and McCann have reported experi-

ments with rhesus monkeys which indicate the possibility that the liver may be protected against a potent yellow fever virus by the oral administration of choline chloride. It must be pointed out that these findings have been made on protein depleted or poorly nourished animals. According to Drill and Loomis (1946) no protection is given by methionine against experimental liver damage due to carbon tetrachloride when normal diets are administered.

The extent to which clinical cases of liver disease in man owe their origin and course to lipotrope deficient diets cannot be stated yet with any assurance. Among the poor natives of India, Africa and China, subsisting on low protein diets, cirrhosis of the liver is extremely common. Cirrhosis of the liver has been found in four out of five autopsies performed on male Bantu at the Johannesburg General Hospital. The diet of the Bantu is almost exclusively maize meal, or mealy meat, supplemented by fermented milk. It has been shown by Gilbert and Gillman, that rats fed on liberal quantities of this diet develop a multitude of lesions, among them cirrhosis of the liver. An analogy might be drawn between the occurrence of cirrhosis among chronic alcoholics and the experimental observations, previously mentioned, that the livers of animals on low protein lipotrope deficient diets are abnormally sensitive to liver toxins including alcohol. Gyorgy has drawn attention to the similarity between the lipotrope deficient lesions the and lesions of eclampsia and acute yellow atrophy. Numerous references in the literature are cited by Himsworth and Glynn illustrating the fatal sensitivity of pregnant women to infective hepatitis. They suggest that the diversion of essential nutriments to the fetus at the expense of the mother may sensitize the mother's liver to the toxic agent of infective hepatitis and predispose to massive hepatic necrosis.

How much are your savings really WORTH?

The *cash value* of your savings is not what counts most. What is important is the amount of *continuous income* they would provide, if your dependents were left without other means of support. In most cases ordinary savings can't provide enough! That is why you need life insurance . . .

Is it important WHICH life insurance company you choose? It is! Evidence of the satisfaction of our policyholders is furnished by the fact that whole families and succeeding generations have entrusted their life insurance programs exclusively to The Mutual Life of Canada, and each year approximately 35% of its new business comes from policyholders. Ask your Mutual Life of Canada representative to explain the special features of this Company.

Low Cost Life Insurance Since 1869

THE MUTUAL LIFE OF CANADA

HEAD OFFICE • WATERLOO, ONTARIO

Feature

C. L. RODGERS, Editor

MEDICAL PRACTICE IN CHINA

By Dr. Jean Millar, as told to C. L. Rodgers

At the rate at which medical students are being graduated in China today, it would take three hundred years to produce enough doctors to come up to the ratio of minimal medical care in Canada. Twenty-nine grade A medical colleges were functioning in China before War enveloped the country. Of these, twenty-eight were either forced to temporarily terminate all teaching, or evacuate to other parts of the country. Thus, one alone, the West China Union University, remained on its Campus and carried on throughout the War. To it went several entire staff and student bodies as refugees from other colleges.

And so hostilities markedly interrupted medical education in China. At the present time readjustment is unbelievably difficult and reorganization and rebuilding are proceeding under extreme handicaps. However, in more recent years the Government has been taking increasingly greater interest in medical education, and as schools are reopened and equipped their needs will be met to an accelerating degree. By fellowships and Government grants many Chinese are now being sent abroad for post-graduate study in order to better prepare themselves for the teaching positions they will assume upon their return. Dr. Bert Yang has spent two and a half years at the Royal Victoria Hospital in Montreal and was the first to receive the Diploma in Urology and Surgery there. He is now in Toronto and will return shortly to the surgical staff of the West China Union University. His wife is also here doing post-graduate work in Obstetrics. In this way more and more Chinese are assuming important teaching positions and the level of medical education on the whole is being gradually raised.

By 1941 there were 235 mission hospitals in China. During the Sino-Japanese War these hospitals supplied four-fifths of the total number of beds available for civilians in Free China. During a normal year the mission hospitals in China treat about four million out-patients and one-quarter million in-patients. To cope with the high number of afflicted, there are only about 12,000 medical doctors, 6,000 nurses, and less than 500 qualified dentists in the whole country. (Canada, with fewer than twelve million people, has about 11,000 medical doctors, 25,000 nurses and 7,000 dentists.) The number of hospital beds at the outbreak of War was 38,000. It has been suggested by the American Hospital Association that an adequate provision would be at least one doctor per 1,500 population and five

---

Dr. Jean Millar, who has spent the past year at the Toronto General Hospital on the staff in Anaesthesia, has devoted 15 years to medical practice in China and intends to return this spring to teach Anaesthesia at the West China Union University Medical College.

The following rambling comments are excerpts from an interview with Dr. Millar during which she briefly reviewed some of her personal experiences and outlined present day medical and health conditions in China.

hospital beds per 1,000 persons. On this basis China ought to have 300,000 doctors and 2,225,000 hospital beds! With twice the incidence of disease, even these enormous numbers would be quite inadequate. Then we must remember, too, that 84 per cent of China's population is rural and that the poverty of both rural peasantry and urban workers renders them incapable of paying for private medical care. Hence, it is generally agreed that in China the only solution of the health problem is state medicine; this is now the declared aim of the Government. Thus China is being compelled to pioneer in a field where her medical mentors in Europe and America have not ventured very deeply. And at the same time she still has to contend with her ancient superstitions and the opposition of those who live by practising the old systems.

Superstitions, which in many cases block the progress of modern methods, must be vigorously combatted. Examples of these are seen every day. For instance, the Chinese believe that they must enter the other world in full possession of all their anatomical parts. Thus amputations, which often are imperative to save life, are refused, or if a limb is amputated it must be kept and placed with its owner at burial. A prominent superstition is that the spirit of a dead snake will enter the body of a person who killed it. Many a death occurs in hospitals because the patient, previous to admission, was treated by a Chinese "Medicine Man" and was given lethal mixtures of ancient potent herbs in an attempt to kill the spirit of the snake. Children die because of old modes of treatment rather than of diseases they contract. Thus babies enter the hospitals with throats torn by a midwife who has scratched out the "evil spirits" from the infant. Often a patient is admitted with burned areas upon its abdomen, placed there in an attempt to treat some abdominal condition. During a measles epidemic children die by the thousands, not due to the measles, but to the ancient methods of treatment with too potent herbs. Therefore education of the public is greatly needed to curb the results of using age old remedies.

One half of all children born alive are dead within their first year! Dysentry, pneumonia, tetanus, malnutrition, and as stated above, bad treatment aggravating existing conditions, are the chief causes of death.

Chinese medicines are taken by the bowl-full. Thus when the Chinese see that Western medicine is handed out in such small amounts as tablets, they have great respect for its potency. A Western doctor has to treat only a few cases of relapsing fever to make a name for himself in a Chinese community. The "Medicine Man" can do nothing for the wildly irrational feverish patient. Within twenty-four hours of treatment by a doctor the patient is rational and feeling well. What a great impression this makes on the family and friends! The advent of sulphas also has proved a great weapon in increasing confidence in Western medicine.

In order to carry out scientific methods in treating the sick, large modern institutions are not absolutely essential. Much can be done even in primitive thatched-roof hovels. By boiling instruments, towels and gloves, operations and deliveries compatible with modern hospital methods can be performed. For two years during the War Dr. Millar was the only doctor in a large crowded village that

was two days' journey from the nearest hospital. Here she set up a clinic in a small hut that boasted a mud floor, a mud stove, and bamboo partitions dividing it into waiting room, consultation room, and operating room. Many major operations were performed there.

Dr. Millar remembers one woman who struggled to the Clinic one day suffering terribly with an unbelievably rotten gangrenous hand. In the presence of a crowd of suspicious, curious Chinese (as was the custom), the hand was amputated. Three weeks later the patient could be seen along the street carrying a market basket with her stump. A very wealthy Chinese official, who had cirrhosis of the liver, came to the Clinic regularly. In the presence of the usual crowd, Dr. Millar would do an abdominal paracentesis, draining off a pail full of fluid. Another very wealthy Chinese gentleman arrived at the Clinic one evening with his infant child, the only son. The baby had sclerema neonatorum, a dreaded and almost invariably fatal condition. Upon duly warning the father, Dr. Millar attempted treatment, wrapping it in warm clothing and feeding it milk, sugar and brandy by duodenal tube. After two weeks of meticulous care it was returned to its adoring father, healthy and happy.

Every one in China has worms. Santonin and castor oil always produce results. After this treatment, Dr. Millar has often seen the patient lying in a bed full of worms that have been passed.

Yet another patient was a pregnant woman who had been stabbed in the abdomen by her husband. The wound was deep enough to incise the uterus to such an extent that the child was visible. Caesarian was performed and both mother and child returned to loving and repentant husband two weeks later.

These are examples of the amazing work done today in China under even the most primitive conditions.

It is admitted that hospitals do great work in healing those few cases that enter their doors. However, Dr. Millar believes that much more important is the public health program and education of the people. At the present time the Chinese Government, in association with many medical organizations in China, is building up a public health program. This is making great strides and is being recognized by the Chinese communities as having high potential value towards the improved health standards of the Chinese people.

RECENT ACCESSIONS TO THE MEDICAL READING ROOM

Advances in enzymology and related subjects. vol. 6, 1946.
Adriani, J.: The chemistry of anaesthesia. 1946.
Aitken, R. S.: The problem of lupus vulgaris. 1946.
American Congress on Obstetrics and Gynecology. Transactions of the 2nd Congress. 1942.
Ashdown, A. M. & E. Bleazby: Anatomy, physiology, and hygiene; a textbook for nurses. ed. 4, 1945.
Arey, L. B.: Developmental anatomy, ed. 5. 1946.
Bicknell, F. & Prescott, F.: The vitamins in medicine. ed. 2. 1946.
Bishop, P. M. F.: Gynæcological endocrinology for the practitioner. 1946.
Corwin, E. H. L.: The American hospital. 1946.
Corner, G. W.: Attaining manhood. 1938.
Courville, C. B.: Pathology of the central nervous system, ed. 2. 1946.
Cowdry, E. V. (ed.): Problems of ageing, ed. 2. 1942.
Cutting, W. C.: A manual of clinical therapeutics. 1943.
Cullis, W. and Bond, M.: The body and its health. 1946.
Campbell, J. D.: Everyday psychiatry. 1945.
Curtis, A. H.: A textbook of gynecology, ed. 5. 1946.
Elwyn, H.: Diseases of the retina. 1946.
Farrell, J. T.: Roentgen diagnosis of diseases of the gastrointestinal tract. 1946.
Fenichel, O.: The psychoanalytic theory of neurosis. 1945.
Fleming, (Sir) Alexander (ed.): Penicillin, its practical application. 1946.
Friedenwald, H.: Jewish luminaries in medical history. 1946.
Galen: On medical experience; 1st ed. of the Arabic version with English translation and notes by R. Walzer. 1946.
Green, D. E. (ed.): Currents in biochemical research. 1946, December 21, 1946.
Harrington, M.: The management of the mind. 1945.
Herndon, R. F.: An introduction to essential hypertension. 1946.
Herrick, A. D.: New drugs. 1946.
Kaplan, O. J.: Mental disorders in later life. [1945].
Keers, R. Y. and Rigden, B. G.: Pulmonary tuberculosis. 1945.
King, E. J.: Micro-analysis in medical biochemistry.
Lawrence, J. S.: The sulphonamides in theory and practice. 1946.
Macintosh, R. R.: Essentials of general anaesthesia. ed. 3, 1945.
Manson, (Sir) Patrick: Tropical diseases. ed. 12, 1945.
Mitchell, P. H.: A textbook of biochemistry. 1946.
Muralt, A. von: Klimaphysiologische Untersuchungen in der Schweiz. I. 1944.
Mustard, H. S.: Government in public health. 1945.
Napier, L. E.: The principles and practice of tropical medicine. 1946.
Peters, C. A. (comp.): Free medical care. 1946.
Peters, J. P. and Van Slyke, D. D.: Quantitative clinical chemistry. I.—Interpretations. ed. 2, 1946.
Polyak, S. L.: The human ear in anatomical transparencies. 1946.
Porter, J. R.: Bacterial chemistry and physiology. 1946.
Scherf, D. and Boyd, L. J.: Clinical electrocardiography, ed. 2. 1946.
Smithers, D. W.: The X-ray treatment of accessible cancer. 1946.
Steindler, A. and Marxer, J. L.: The traumatic deformities and disabilities of the upper extremity. 1946.
Stern, B. J.: Medical services by government. 1946.
Stitt, E. R.: Diagnosis, prevention and treatment of tropical diseases, rev. by Richard P. Strong. 2 v. ed. 7, 1944.

Abstracts

C. L. ASZKANAZY, Editor

Contributors

C. L. Aszkanazy
J. Bellamy
W. G. B. Casselman
W. B. Weisbrod

MEDICINE I

Oral Folic Acid Therapy in the Treatment of Pernicious Anaemia. J. Kaufmann and P. G. Schwager. C.M.A.J., vol. 54, No. 6. June 1946.

The work of various investigators is outlined concerning the similarity between folic acid and the growth factor of liver, its anti-anaemic effect on chicks, rats and monkeys, and its synthesis.

The work of Spies on 45 clinical cases demonstrated its possible clinical application to the macrocytic anaemias, leukopenias and thrombocytopenias.

Four cases are presented demonstrating the typical fully developed picture of pernicious anaemia plus mild peripheral neuritis and minimal loss of vibration sense and sense of position in the lower limbs. In addition to the routine hospital diet, 40 mgm. of Folic Acid was given daily in divided dosage between meals. Iron was given if hypochromia appeared, and HCl for post-prandial distress. After 3 to 4 days of this treatment, there was definite clinical improvement of all the symptoms. The reticulocyte count reached a peak of 45% on the 9th day; the red count showed a daily increase of 90,000/cmm.; the Hb. a daily 1% increase. The bone marrow showed active normoblastic proliferation and the white count and platelets returned to the normal level. The maintenance dose varied from 5-15 mgm. daily. No toxic allergic manifestations were observed.

The authors believe that the drug, like the liver, stimulates maturation of megaloblasts. It can be used alternatively with liver without producing disturbances.

W. B. W.

MEDICINE II

The Role of the Emotions in the Production of Gastro-Intestinal Disturbances. J. P. S. Cathcart: Can. Med. Assn. J. *55,* 465-470 (1946)

Emotional influences, chiefly those reflecting deep seated conflicts, have definite effects on the gastro-intestinal tract, even to the extent of producing pathological changes as in peptic and special forms of diarrhoea and constipation.

There is a close relationship between anxiety neurosis and peptic ulcer, and between peptic ulcer and so called "gastric neurosis." Psychotherapeutic methods of dealing with anxiety neurosis are equally effective in dealing with peptic ulcer. An unhurried interview with few of the "trappings of professional approach," is

essential. It is essential that the physician avoid imposing too many cautions and restrictions and insisting on too many procedures and rechecks. If facilities permit, group psychotherapy should be used, but never as a complete substitute for individual exploration and therapy. W. G. B. C.

MEDICINE III

VIRAL INFECTIONS OF RESPIRATORY TRACT, THEIR TREATMENT AND PREVENTION. H. A. Reimann: J. Amer. Med. Assn. *132,* 487-493 (1946)

This discussion deals with acute, self-limiting, chiefly airborne diseases of known or presumed viral origin affecting predominantly the respiratory tract and ordinarily called colds, grippe or influenza and with certain newly delineated ones (pharyngitis and/or tonsillitis, febrile, catarrh, and viroid). These are considered under the headings of epidemiology, classification, treatment and preventive measures. The causes of some are known and those of the rest await discovery until final classification is possible. Many preventive and therapeutic measures in common use are in need of revision or deletion. Except for influenza, there are no specific preventive procedures and no specific therapy exists for any infection in the group. Management should be suited to the needs of the patient in order to relieve discomfort, to prevent complications without impeding the natural process of recovery and to minimize the spread of infection to others. W. G. B. C.

PAEDIATRICS I

IMMUNIZATION IN CHILDREN. J. H. B. Grant: Can. Med. Assn. J. *55,* 493-497 (1946)

Excellent results have been obtained from the active immunization against smallpox and typhoid and paratyphoid fevers. One hundred percent immunity can be produced if vaccination and re-vaccination are carefully preformed as needed.

Diphtheria can be prevented in the vast majority of children by the use of toxoid, re-inforced by booster doses every five years.

Whooping cough vaccine is of definite value but there remains the problem of the very young infant. It is stated that infants under six months do not produce sufficient immune reactions to diphtheria toxoid or pertussis vaccine to prevent these disease on exposure, and in the case of whooping cough sixty percent of deaths have occurred by the seventh month.

Scarlet fever immunization has a very definite place but its acceptance by physicians and parents has not been great. By the use of scarlet fever immunization, one can prevent the systemic damage (to kidneys, heart, etc.) caused by the toxin of the hemolytic streptococcus.

Tetanus toxoid has not yet come into widespread use but it is very effective.

For passive immunization, diphtheria and tetanus antitoxins will effectively prevent these disesase, if given in time. Scarlet fever antitoxin has been replaced to a great extent by the sulfonamides. Convalescent serum has a definite value in measles. W. G. B. C.

SURGERY I

THIOURACIL WILL NOT REPLACE THYROIDECTOMY. A. S. Jackson: Surg. Gynec. and Obstet. *83*, 249-252 (1946)

Jackson believes that thiouracil will not replace thyroidectomy, because if the health of the average patient with toxic diffuse goitre may be restored by surgery within a few weeks there seems little justification for subjecting the patient to prolonged treatment with a dangerous drug. The risk of using thiouracil seems justified in (1) advanced cases of multiple toxic adenoma in which there is no response to iodine; (2) cases of toxic adenoma in which such conditions as myocarditis, fibrillation, hypertension, diabetes, and decompensation are complications; (3) cases of severe toxic diffuse goitre in the very young, the aged, the debilitated and the decompensated; (4) cases of toxic diffuse goitre in which because of pregnancy, previous nerve injury, infection, or other diseases, it may be desired to delay surgery and yet not continue on iodine; (5) cases of iodine fast toxic diffuse goitre; and (6) cases of recurrent or persistent hyperthyroidism. The author's experience with thiouracil has proved encouraging in all these types of cases. Probably the gravest risk in the surgical treatment of hyperthroidism has been brought under control, namely the advanced cases of toxic adenoma in which a two stage thyroidectomy has usually been required. After several weeks of preparation with thiouracil, the author has successfully performed a one stage thyroidectomy in these cases. Thiouracil considerably reduced the risk in several cases in which the systolic blood pressure was greater than 225 and in which the threshold of cardiac reserve was small. Jackson concluded that thiouracil will supplement but not supplant surgery in the treatment of toxic goitre.

W. B. G. C.

SURGERY II

Jenkins H. P. and Janda R. "Studies on the Use of Gelatin Sponge or Foam as an Hæmostatic Agent in Experimental Liver Resections and Injuries to Large Veins" Annals of Surgery *124* (*4*): 952 Nov. 1946

The authors report experimental work performed on dogs in order to investigate the gelatin sponge, described by Correll and Wise in 1945. The livers of 12 dogs were exposed aseptically and pieces snipped of with scissors. Then gelatin sponge, which had been moistened in saline and squeezed between layers of gauze, was applied to the bleeding site with firm pressure for 5 to 10 minutes. No suturing was used, but in some cases fresh sponge had to be applied.

2 of the animals died of bile peritonitis on the 4th and 5th day, the others were sacrificed from 2 days to 6 weeks after the operation and post mortems performed. During the first 4 days, the sponge was red and friable and fixed to the liver by fibrinous adhesions. After 2 weeks, the sponge was covered by adhesions attaching it to the omentum and other adjacent structures. By the 4th week, the sponge was hardly recognizable and the liver well healed over. Microscopically there was a little leucocytic activity in the early stage, soon followed by active fibroplasia invading the

sponge which resulted in absorption of the sponge and formation of connective tissue.

Large veins in 36 dogs were exposed and stabbed or pieces of the wall excised. Application of the gelatin sponge stopped the bleeding in all but two cases. The animals were sacrificed and examined. After 8 to 12 days, the wound began to close over and after 3 weeks, an endothelized scar had formed. Thrombi were of uncommon occurrence and in no case did complete occlusion result.

The sponge was used in 76 patients with good results for various types of troublesome bleeding.

The authors believe that if the sponge can be made somewhat tougher so that it can be stiched to the tissues and is not so easily liquefied by leucocytes, it will prove of great value in liver resections for tumors. C. L. A.

SURGERY III

Turnbull F. "Observation on the Surgical Relief of Pain in Cancer" C.M.A.J. vol. 55 Sept. 1946.

The author describes the operation of cordotomy for the relief of intractable pain. Intractable pain is defined as pain requiring at least 1 daily dose of narcotic drug for alleviation, i.e. at least 1 gr. of Codeine or opiates or demerol in any dose. The operation is indicated, when the intractable pain has been present for over a month and when the patient does not show signs of terminal cachexia.

Cordotomy is performed for the relief of pain situated below the mid-thorax and is commonly done before palliative local operation. There is the risk of diminished sensitivity of bladder and possible weakness of legs. The relief of pain must be absolute to justify the operation. J. B.

UROLOGY I

Schacht F. W. and Barlur K. E. "Sulphathiazole Suppositories in the Treatment of Vulo Vaginitis in Children" J. Urol. vol. 56 No. 4, Oct. 1946.

The authors state that mixed bacterial infection is the aetiological agent in most cases.

In their cases, the symptoms and pathological changes were not severe, consisting mainly of persistent foul vaginal discharge. Digital rectal examination was made to rule out the presence of foreign bodies in the vagina. Cultures and smears were made.

Local hygiene and proper toilet habits were important adjunctives in therapy. The suppositores consisted of 7½ grs. sulphathiazole powder incorporated in cocoa butter. In accord with instructions to the mothers, these suppositories were introduced into the vagina every night. On the average, 8 weeks were required before the discharge stopped completely and the vaginal mucosa appeared normal again. Cultures were repeatedly negative.

The only toxic manifestation was a slight skin rash in one case.

W. B. W.

OTOLARYNGOLOGY I

Atkinson M. "Menière's Syndrome: The Basic Fault" Archives of Otolaryngology *44 (4): 385* Oct. 1946.

The author proposes the theory that the basic cause of Menière's syndrome is a dysfunction of the capillaries. Only 10 autopsies have been described in the literature and in these the chief feature was a gross dilatation of a large part of the endolymphatic system. This may be caused by deficient absorption of the endolymph from the saccus endolymphaticus, excess production at the stria vascularis or a combination of both factors. The first factor is ruled out by the normal appearance of the saccus endolymphaticus. The stria also appears normal, but increased capillary permeability is a functional, not an organic disorder.

Further evidence is the fact that hyperhydration brings on attacks and dehydration abolishes them. A low salt diet and such diuretics as Amm. Chloride and Potassium Ions are valuable in the treatment.

Benefit is often derived by patients from the intravenous injection of histamine. The author divides sufferers into 2 groups. One of these can be shown to be very sensitive to intradermal injection of histamine with resulting capillary leakage. Intravenous histamine is supposed to desensitize such cases and thus to improve them. The other group responds normally to histamine. Here, the author believes, vasoconstriction with resulting anoxaemia and capillary leakage occurs, which is relieved by the vasodilating action of histamine.

Cases in which allergy, Vit. C deficiency and toxic labyrinthitis were believed to be the causative factor, can all be fited into the theory of increased capillary permeability.

C. L. A.

INDEX

Title	*Author*	*Vol.*	*No.*
Anaesthesia, Continuous, Caudal, in Obstetrics	E. E. Cleaver	XXI	4
Anaesthetics, Local, Relationship between the Toxicity, Potency, Acquired Sensitivity of	G. H. W. Lucas	XXIII	5
Antibiotics	P. Greey	XXIII	5
Anxiety Neuroses	S. Greenhill	XXI	1
Arterial Disease, The differential Diagnosis of Peripheral	F. H. Davis	XX	5
Aviation Medicine	G. W. Manning	XXIV	1
Bladder and Urethra, Traumatic Rupture of	D. C. Robertson	XX	6
Blast Injury, Part I	W. R. Harris	XXII	3
Blast Injury, Part II	K. F. Clute	XXII	4
Bone Formation, Physiology of	N. R. Stephenson	XXII	6
Bright's Disease	A. E. Parks	XX	3
Burns	K. M. Johnston	XXI	5
Burns, Recent Advances in the Treatment of	R. I. Harris	XX	4
Calculi, Renal	R. F. Warren	XX	3
Canadian Intern Board	R. B. Andrew	XXIII	4
Carbon Monoxide Anoxemia	M. L. Bunker	XXIII	3
Carcinoma of the Prostate	J. Firstbrook	XXI	6
Causation in Pathology	T. D. Muir	XXIV	2
Cervix, Cancer of	C. A. F. Moes	XXIII	6
Chest Wall and Intrathoracic Structures, Injuries to	R. M. Janes	XXIII	6
Crush Syndrome	K. F. Clute	XX	6
Digitalis, Pharmacology of	J. K. W. Ferguson	XXIV	2
Death, Sudden	W. L. Robinson	XXIII	6
Desert Surgery, Part I	Maj.-Gen. Ogilvie	XXI	3
Desert Surgery, Part II	Maj.-Gen. Ogilvie	XXI	4
Diabetes, The Biochemistry of	M. O'Sullivan	XXI	1
Diabetic Patient, Method of Treatment of	K. T. G. Moller & J. R. Corriston	XXI	3
Duodenal Ulcer	T. A. J. Duff	XX	2
Edema	R. J. Slater	XXIII	1
Electric Shock Therapy in Mental Disorders	D. Currie	XXIII	1
Electrocardiograms, The Interpretation of	F. C. Hamilton	XXII	3
Electron Microscope	L. T. Newman	XX	5
Endometriosis	H. I. Brown	XXIII	3
Epilepsy, On	P. Allen	XXII	6
Erythroblastosis and the Rh Factor	V. J. Freeman	XXII	1
Feeble Minded, The Education of	H. G. Hazel	XX	4
Feet, The Comparative Anatomy of, and its Relation to Functional Disturbance		XX	2
Fractures, Compound	E. F. Routely	XX	5
Fractures, Healing of	H. B. Stewart	XX	2
Fractures in General	J. C. McLeish	XXI	2
Fractures, Non-Union of	F. I. Lewis	XXII	5
Fractures of the Calcaneum	J. V. Basmajian	XXII	6
Gastro-Intestinal Motility	A. S. Deacon	XXII	5
Genito-Urinary Tract, Pain from	J. C. McClelland	XXII	2
Glucose Tolerance Test	K. T. G. Moller & J. R. Corriston	XXI	3
Hands, Infection in	J. H. Couch	XXII	4
Headaches, Part I	W. T. Clark	XXI	1
Headaches, Part II	W. T. Clark	XXI	2

Title	*Author*	*Vol.*	*No.*
Hernia, When is	H. F. Robertson	XX	1
Histidine Pregnancy Test	A. H. James	XXI	2
How to Write an Article	M. E. Couch	XXIV	1
Hydronephrosis	L. P. Todd	XX	6
Hypertension, The Pathogenesis of	R. M. Bremner	XXIII	1
Infantile Diarrhea	D. E. Ross	XXIII	4
Influenza	S. E. O'Brien	XXIII	4
Injuries of the Thorax	J. H. Carson	XXII	1
Intestinal Obstruction	H. Loeb	XXI	5
Intestinal Obstruction, The Influence of Experimental Study on Clinical Practice in		XX	1
Isotopes, Tracer in Radiotherapy	N. B. Keevil	XX	4
Juxtaglomerular Apparatus	R. J. Holden	XXI	1
Liver Function Tests, Part I	R. D. Hawkins	XXIII	4
Liver Function Tests, Part II	R. D. Hawkins	XXIII	5
Lump in the Neck	J. W. Scott	XXII	6
Lymphglands of the Head and Neck and Extremities	J. V. Basmajian	XX	5
Medical Glee Club	J. M. Finlay	XXIII	5
Military Surgery, Application to Civilian Practice	F. G. Kergin	XXIII	5
Muscular Contraction, Chemistry of	J. B. Firstbrook	XX	4
Nerve Impulses, The Chemical Transmission of	W. H. Allemang	XXI	3
Oculomotor Nerve, Some Important Points in the Anatomy	E. A. Linell	XXII	4
Oesophagus, History in Disease of	F. E. Cleaver	XXI	4
Ophthalmic Indications of Systemic Disease	A. J. Elliot	XXIV	1
Osteochondritis Dissecans	H. J. Sullivan	XX	2
Osteomyelitis, Effect of Sulphonamides on Acute	W. T. Clark	XXI	2
Pain	L. M. Bunker	XXIII	1
Penicillin	D. E. Hutcheon	XXI	6
Pitch Discrimination	R. C. Partridge	XXII	6
Pneumonia, Primary Atypical, Part I	W. T. Clark	XXI	3
Pneumonia, Primary Atypical, Part II	W. B. Arnup	XXI	3
Psychiatry, Shock Therapy in	R. M. Bremner	XXI	5
Psychiatry, Shock Therapy in	B. Berris	XXII	1
Psychonfurosis, The Management of	C. W. Taylor	XXIV	1
Psychosomatic Medicine	C. H. Cahn	XXII	3
Pulmonary Tuberculosis and the General Practitioner	M. S. Lauder	XXIV	2
Rectum, Carcinoma of	A. H. H. Malcolm	XXIII	6
RH Factor and Erythroblastosis Fetalis	R. Slater	XXIII	3
Small Latin and Less Greek	J. C. B. Grant	XXIV	2
Skin Grafting	L. S. Davies	XXII	2
Spleen as a Surgical Problem	R. M. Bremner	XXII	2
Sulphonamides, Fatal Results of	B. Berris & M. L. Snider	XXI	2
Thiouracil	K. A. Brown	XXI	6
Thyrotoxicosis	T. Y. Chang	XXIII	3
Tumours of the Breast, Clinical Diagnosis of	J. C. Gray	XXII	4
Use of Pituitary Extracts in Obstetrics	O. Kofman	XXIII	4
Varicose Veins in the Lower Limb	W. Kalant	XXIV	1
War Amputations	R. I. Harris	XXI	6

"GASTRIC ALKALINE"

(C.T. No. 241 "Frosst")

As a Neutralizing Agent in Simple Hyperacidity: For such conditions as acidity from the onset of common colds and grippe, improper diet, excessive eating or drinking, etc.

As a Treatment in the Early Stages of Gastric or Duodenal Ulcer: As a part of the complete treatment—rest, proper diet, etc.—to neutralize the gastric or duodenal acids which retard healing. Its administration is desirable whether the ulcer is suspected or definitely diagnosed.

FORMULA:

Each tablet renders available:

Sodium bicarbonate	5 gr. (0.324 G.)
Bismuth subcarbonate	5 gr. (0.324 G.)
Magnesium carbonate	5 gr. (0.324 G.)
Oil peppermint	q.s.

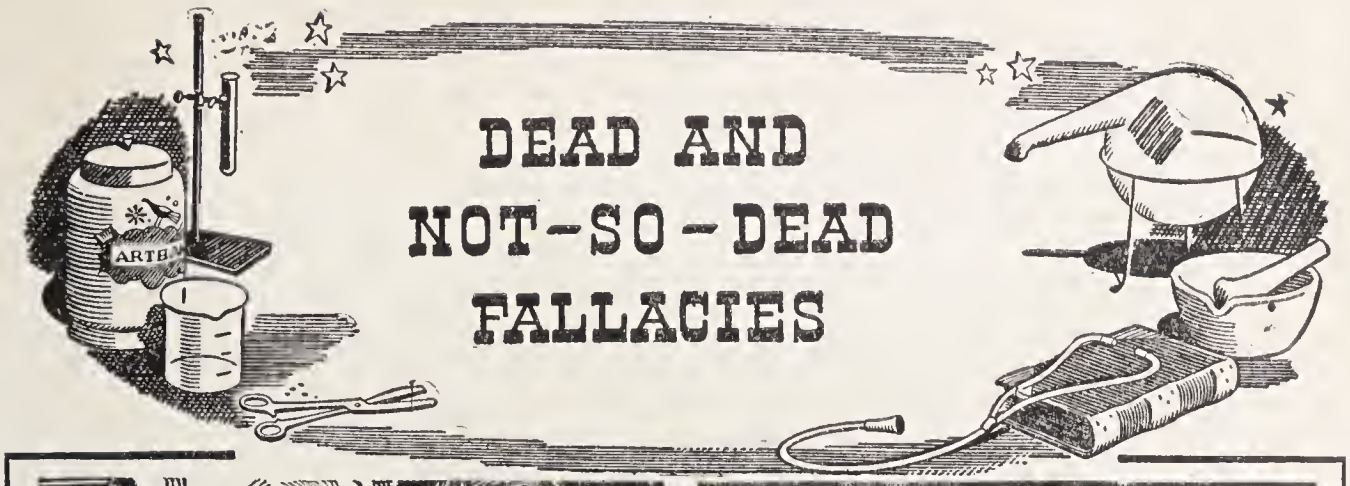
MODES OF ISSUE: Bottles of 100 and 500 Tablets

DOSAGE:

One to four tablets. These tablets may be allowed to disintegrate in a quantity of water and then be administered in the form of a flaky mixture.

Frosst
SINCE 1899
THE SYMBOL OF PROGRESS IN PHARMACEUTICAL RESEARCH

Charles E. Frosst & Co.
MONTREAL CANADA



DEAD AND NOT-SO-DEAD FALLACIES

During the plague of 1665, Londoners lit bonfires in the streets, thinking this would "purify the air." They also killed all dogs, which they blamed for spreading the disease. Rats, the real offenders, were left unharmed.

Seeing rust on the outside of a can, leads many people, even in this enlightened day and age, to suspect that the food inside is contaminated. The truth is that, unless the rust has eaten through the metal, the food is perfectly safe for consumption.

CANCO **AMERICAN CAN COMPANY**
MONTREAL HAMILTON TORONTO VANCOUVER

Now available on request—
"THE CANNED FOOD REFERENCE MANUAL"

—a handy source of valuable dietary information. Please fill in and mail the attached coupon **now.**

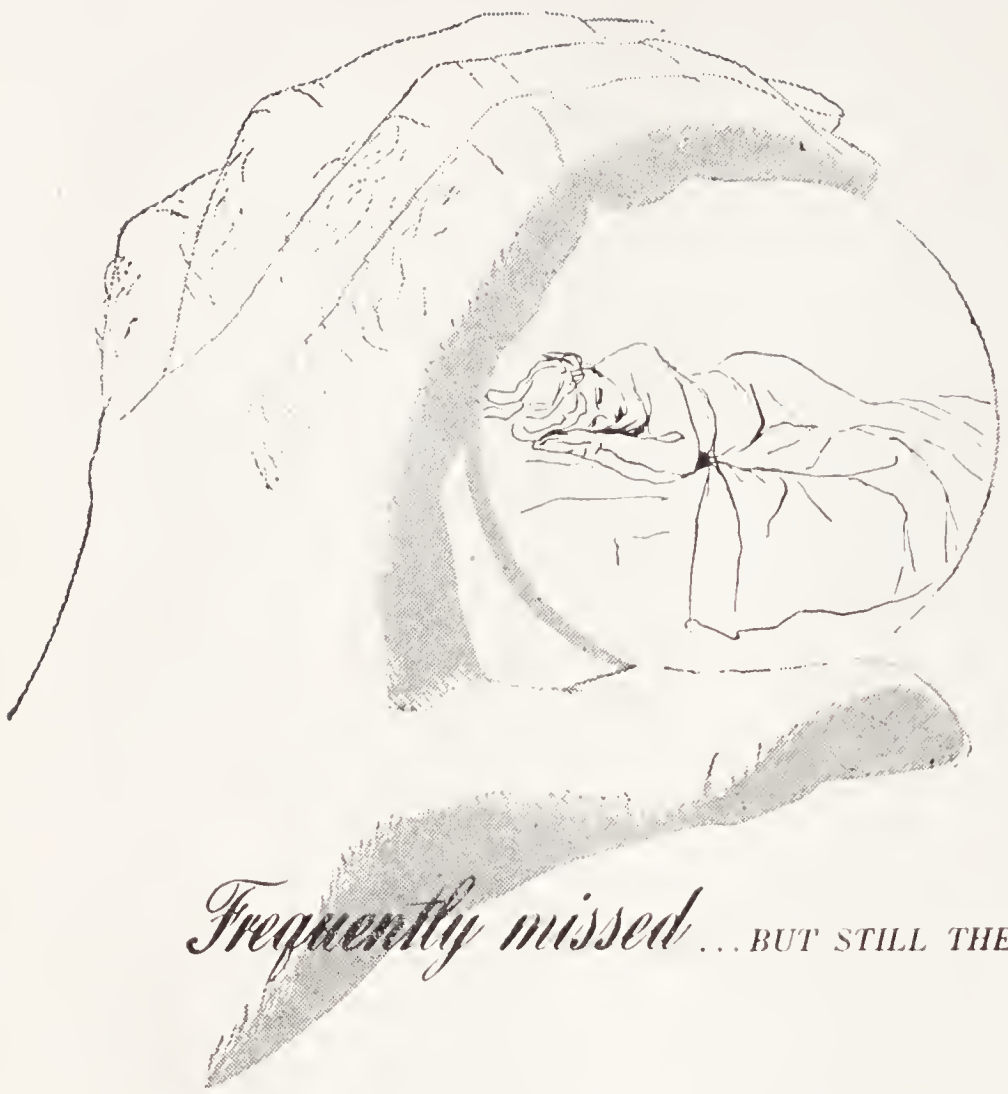
AMERICAN CAN COMPANY
Medical Arts Building, Hamilton, Ont.
Please send me the new Canadian edition of "THE CANNED FOOD REFERENCE MANUAL," which is free.

Name.....

Professional Title.....

Address.....

City.....Province.....



Frequently missed ... BUT STILL THERE

"The diagnosis of deficiency disease," states Jolliffe, "is frequently missed because it is not looked for."

But once recognized, the sick patient with mixed vitamin deficiencies must be treated with the essential vitamins in doses of therapeutic magnitude. No simple multiplication of maintenance multi-vitamin preparations is practical — for there is no fixed ratio between the doses for therapy and those for maintenance.

For doses of true therapeutic magnitude prescribe SQUIBB THERAPEUTIC FORMULA. A single capsule contains these massive doses:

Vitamin A	25,000 units	5 times
Vitamin D	1,000 units	1¼ times
Thiamine HCl	5 mg.	2½ times
Riboflavin	5 mg.	2 times
Niacinamide	150 mg.	7½ times
Ascorbic Acid	150 mg.	2 times

maintenance level recommended by the Food and Nutrition Board of the National Research Council

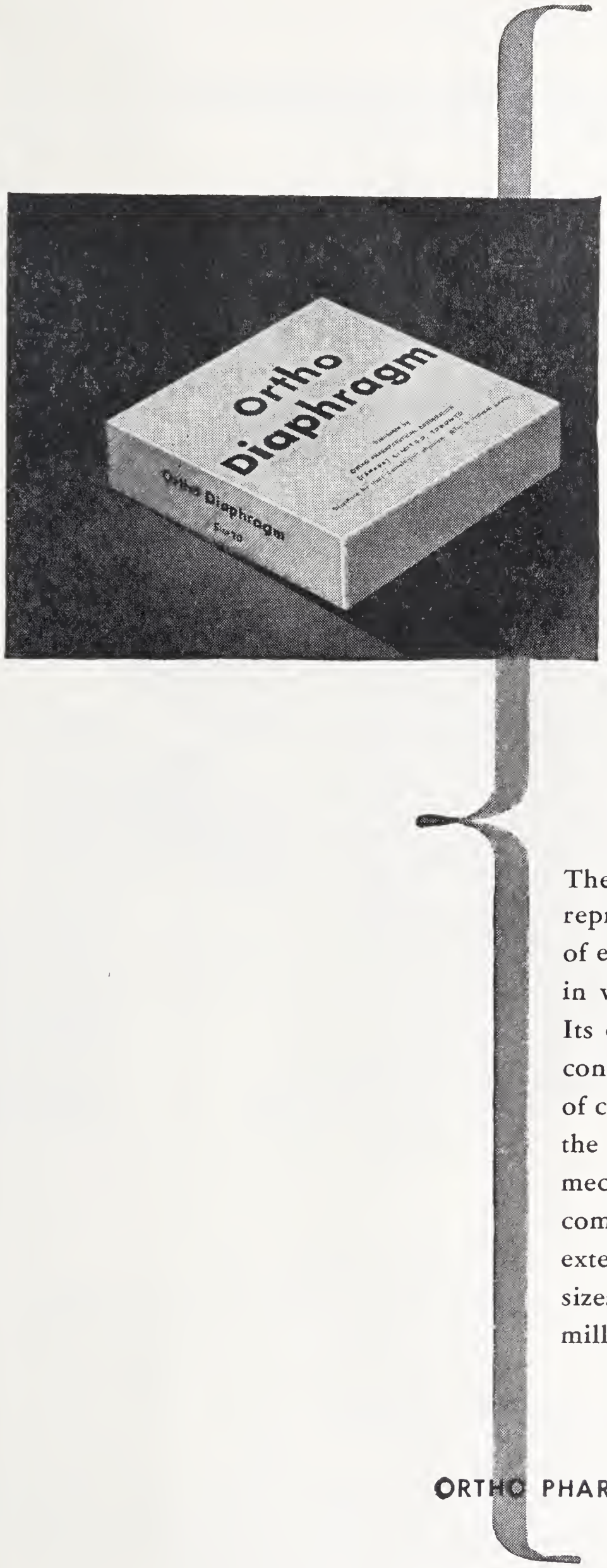
For literature write E. R. Squibb & Sons of Canada Limited, 36 Caledonia Road, Toronto

SQUIBB Therapeutic Formula

VITAMIN CAPSULES

174A

E. R. SQUIBB & SONS OF CANADA LTD., 36 CALEDONIA ROAD, TORONTO



designed by

gynecologists

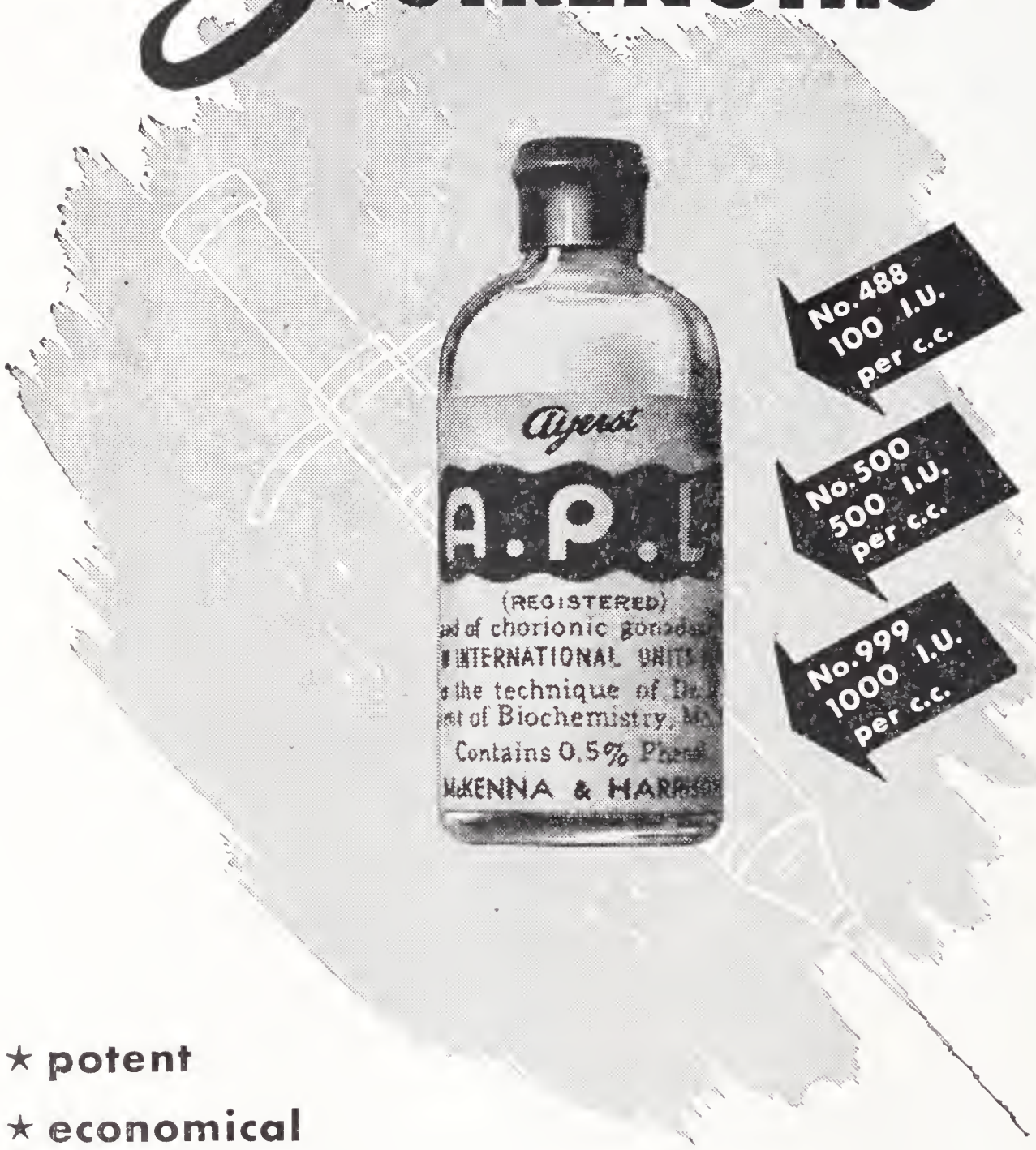
and engineers

The **ORTHO DIAPHRAGM** represents a new high standard of efficiency and convenience in vaginal diaphragms. Its design, materials and construction are the result of careful planning to achieve the requirements of an effective mechanical barrier, and affords comfort for the patient through extended use. Available in sizes ranging from 55 to 95 millimeters.

ORTHO PHARMACEUTICAL CORPORATION
(CANADA) LIMITED
TORONTO

Brand of chorionic gonadotrophin in

3 STRENGTHS



★ **potent**

★ **economical**

★ **painless on injection**

For the treatment of cryptorchidism, Frohlich's syndrome, hypogonadism, menorrhagia and metrorrhagia.

AYERST, McKENNA & HARRISON LIMITED 426

Biological and Pharmaceutical Chemists • MONTREAL, CANADA